

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
24 October 2002 (24.10.2002)

PCT

(10) International Publication Number
WO 02/084301 A3

(51) International Patent Classification⁷: **G01N 33/92**,
C12Q 1/60

(21) International Application Number: PCT/CA02/00489

(22) International Filing Date: 12 April 2002 (12.04.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/283,424 12 April 2001 (12.04.2001) US

(71) Applicants (for all designated States except US): **XENON GENETICS, INC.** [CA/CA]; 3650 Gilmore Way, Burnaby, British Columbia V5G 4W8 (CA). **UNIVERSITY OF BRITISH COLUMBIA** [CA/CA]; 2194 Health Sciences Mall, Vancouver, British Columbia V6T 1Z3 (CA).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **ZHANG, Lin-Hua** [CA/CA]; 3352 East 25th Avenue, Vancouver, British Columbia V5R 1J8 (CA). **HAYDEN, Michael, R.** [CA/CA]; 4484 West 7th Avenue, Vancouver, British Columbia V6R 1W9 (CA). **NEWMAN, Scott, M.** [US/CA]; 4420 Nanaimo Street, Vancouver, British Columbia V5N 5J3 (CA).

(74) Agent: **MBM & CO.**; P.O. Box 809, Station B, Ottawa, Ontario K1P 5P9 (CA).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
5 June 2003

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 02/084301 A3

(54) Title: SCREENING ASSAY FOR AGENTS MODULATING ACTIVITY OF THE ABCA1 PROTEIN

(57) Abstract: High throughput screening assays for agents capable of modulating lipid metabolism are disclosed. Such agents are detected by their ability to modulate the activity of proteins interacting with, and modulating the activity of, the protein expressed by the ABCA1 (called CERP - or cholesterol efflux regulating protein). Methods of treating disorders of lipid metabolism, especially those involving elevated levels of phospholipid or cholesterol, are also described.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 02/00489

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/92 C12Q1/60

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 00 55318 A (UNIV BRITISH COLUMBIA ;XENON BIORESEARCH INC (CA)) 21 September 2000 (2000-09-21) claims 47,52,54-57 ---	1-3, 5-17,48
A	KISS H ET AL: "A novel gene containing LIM domains (LIMD1) is located within the common eliminated region 1 (C3CER1) in 3p21.3." HUMAN GENETICS. GERMANY DEC 1999, vol. 105, no. 6, December 1999 (1999-12), pages 552-559, XP002222707 ISSN: 0340-6717 abstract; figure 2 --- -/--	1-3, 5-17,48



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

28 November 2002

Date of mailing of the international search report

28.03.03

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+31-70) 340-3016

Authorized officer

Luis Alves, D

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 02/00489

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ORAM J F ET AL: "ABCA1 IS THE CAMP-INDUCIBLE APOLIPOPROTEIN RECEPTOR THAT MEDIATES CHOLESTEROL SECRETION FROM MACROPHAGES" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 275, no. 44, 3 November 2000 (2000-11-03), pages 34508-34511, XP000990439 ISSN: 0021-9258 abstract -----	1-3, 5-17,48
P,A	SANTAMARINA-FOJO SILVIA ET AL: "Regulation and intracellular trafficking of the ABCA1 transporter." JOURNAL OF LIPID RESEARCH, vol. 42, no. 9, September 2001 (2001-09), pages 1339-1345, XP001120631 ISSN: 0022-2275 abstract page 1341, left-hand column, paragraph 3 -page 1342, right-hand column, paragraph 2 -----	1-3, 5-17,48

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 02/00489

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 18-27, 29-47
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-3, 5-17, 48 (all partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 18-27, 29-47

Independent claim 1 concerns screening methods making use of "an ABCA1-interacting protein (AIP)". Such definition may encompass a large number of proteins and its broadness is not supported by the description, which only provides a limited number of proteins, which were merely shown to be expressed in certain cell lines in which ABCA1 is expressed. Therefore, claim 1 and dependent claims 2 to 17 lack support in the description (Article 6 PCT) and a meaningful search is only possible for the methods making use of the proteins identified in the application, ie, the proteins as listed in claim 2.

Claim 18 concerns a screening process which involves administering to an animal a compound which is the result of the screening methods defined in claims 1 to 17.

However, said compound is not characterized in any way. It is attempted to define said compound merely by reference to a screening method. Thus, said claim lacks clarity (Article 6 PCT) to such an extent that a meaningful search is not possible.

The same objection (Article 6 PCT) applies to independent claim 23, for the same reasons, as well as to dependent claims 19 to 22, 24 to 27 and 29 to 43.

Independent claims 44 to 47 concern methods of treatment comprising the administration of a compound which is the result of the screening processes defined in claims 25 and 20, respectively. As reasoned above, a meaningful search is not possible for the subject-matter of claims 20 and 25. For this reason, and for analogous reasons as above concerning a lack of clarity of the claims in which it is attempted to define compounds merely by reference to screening process, a meaningful search for the subject-matter of claims 44 to 47 is not possible (Article 6 PCT).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by LIMD1 (Seq id no 1).

2. Claims: 1 , 2, 4-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by KIAA0528.

3. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by RAD23A.

4. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by PDI-ERp58.

5. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by OAZ1.

6. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by LOC51691.

7. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by PFDN5.

8. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by My001.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

9. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by RP4-744I24.

10. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by KPNB1.

11. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by Bip/Grp78.

12. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by TPT1.

13. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by NAP1L1.

14. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by E46.

15. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by PRB4.

16. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by Rhoip2.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

17. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by Ubiquinone.

18. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by AK011474.

19. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by CGI-24.

20. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by TCP1.

21. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by IFITM2.

22. Claims: 1-3, 5-17, 48 (all partially)

Screening methods comprising determining the activity of ABCA1 in the presence of a test compound which has been contacted with a polypeptide encoded by .

INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/CA 02/00489

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0055318 A	21-09-2000	AU 3832700 A	04-10-2000
		DE 1100895 T	06-09-2001
		EP 1100895 A	23-05-2001
		AU 1291901 A	26-03-2001
		EP 1239848 A	18-09-2002
		WO 0115676 A	08-03-2001
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